Table 20: Four Pages

Table 20. Drug Interactions Between Antiretrovirals and Other Drugs: PIs, NNRTIs, and NRTIs

Drug Interactions Requiring Dose Modifications or Cautious Use			
Drugs Affected	**Indinavir (IDV)**	**Ritonavir (RTV)**	**Saquinavir† (SQV)**
ANTIFUNGALS			
Ketoconazole	Levels: IDV ↑ 68%. Dose: IDV 600 mg tid.	Levels: ketoconazole ↑ 3X. Dose: Use with caution; do not exceed 200 mg ketoconazole daily.	Levels: SQV ↑ 3X. Dose: If ketoconazole dose is >200 mg/day, monitor for excessive diarrhea, nausea, abdominal discomfort and adjust doses accordingly.
Voriconazole	Levels: No significant changes in AUC of azole or IDV (healthy subjects). Dose: Standard	No data, but potential for bi-directional inhibition between voriconazole and PIs, monitor for toxicities	No data, but potential for bi-directional inhibition between voriconazole and PIs, monitor for toxicities
ANTI-MYCOBACTERIALS			
RifampinΣ	Levels: IDV ↓ 89%. Contraindicated.	Levels: RTV ↓ 35%. Dose: No Data. Increased liver toxicity possible.	Levels: SQV ↓ 84%. Contraindicated, unless using RTV+SQV, then use rifampin 600 mg qd or 3x/week.
Rifabutin	Levels: IDV ↓ 32%. Rifabutin ↑ 2X. Dose: ↓ rifabutin to 150 mg qd or 300 mg 3x/week. IDV 1000 mg tid.	Levels: Rifabutin ↑ 4X. Dose: ↓ rifabutin to 150 mg qod. or dose 3x per week. RTV: Standard.	Levels: SQV ↓ 40%. No rifampin dose adjustment unless using RTV+SQV, then use rifabutin 150 mg 3x/week.
Clarithromycin	Levels: Clarithromycin ↑ 53%. No dose adjustment.	Levels: Clarithromycin ↑ 77%. Dose: Adjust for moderate and severe renal impairment.	Levels: Clarithromycin ↑ 45%. SQV ↑ 177%. No dose adjustment.
ORAL CONTRACEPTIVES	Levels: Norethindrone ↑ 26%. Ethinylestradiol ↑ 24%. No dose adjustment.	Levels: Ethinyl estradiol ↓ 40%. Use alternative or additional method.	No data.
LIPID–LOWERING AGENTS			
Simvastatin **Lovastatin**	Levels: Potential for large increase in statin levels. Avoid concomitant use.	Levels: Potential for large increase in statin levels. Avoid concomitant use.	Levels: Potential for large increase in statin levels. Avoid concomitant use.
Atorvastatin	Levels: potential for increase in AUC Use with caution.	Levels: 450% ↑ when administered with SQV/RTV combination. Use with extreme caution.	Levels: 450% ↑ when administered with SQV/RTV combination. Use with extreme caution.
Pravastatin	No Data	Levels: 50% ↓ when administered with SQV/RTV combination. No dose adjustment needed.	Levels: 50% ↓ when administered with SQV/RTV combination. No dose adjustment needed.
ANTICONVULSANTS			
Carbamazepine **Phenobarbitol** **Phenytoin**	Carbamazepine markedly ↓ IDV AUC. Consider alternative agent.	Carbamazepine: ↑ serum levels when co-administered with RTV. Use with caution. Monitor anticonvulsant levels.	Unknown, but may markedly ↓ SQV levels. Monitor anticonvulsant levels.
METHADONE	No change in methadone levels.	Methadone ↓ 37%. Monitor and titrate dose if needed. May require ↑ methadone dose.	No data.
MISCELLANEOUS	Grapefruit juice ↓ IDV levels by 26%. Sildenafil AUC ↑ 3 fold. Use cautiously. Start with reduced dose of 25 mg every 48 hours and monitor for adverse effects.	Many possible interactions Desipramine ↑ 145%, reduce dose. Theophylline ↓ 47%, monitor theophylline levels. Sildenafil AUC ↑ 11 fold. Use cautiously. Start with reduced dose of 25 mg every 48 hours and monitor for adverse effects.	Grapefruit juice ↑ SQV levels. Dexamethasone ↓ SQV levels. Sildenafil AUC ↑ 2 fold. Use a 25 mg starting dose of sildenafil.

* Drugs for which plasma concentrations may be decreased by coadministration with ritonavir: anticoagulants (warfarin), anticonvulsants (phenytoin, divaproex, lamotrigine), antiparasitics (atovaquone).

† Some drug interaction studies were conducted with Invirase®. May not necessarily apply to use with Fortovase.

Σ There are limited data on RTV-SQV and RTV-LPV demonstrating that RTV compensates for rifampin induction. In one small study, higher boosting doses or ritonavir (up to 400 mg per dose) were needed to fully offset rifampin-inducing activity of LPV. Whether RTV can be used to offset rifampin induction of all other protease inhibitors, or whether this therapeutic maneuver is more broadly applicable, requires further study.

Table 20: Four Pages

Table 20. Drug Interactions Between Antiretrovirals and Other Drugs: PIs, NNRTIs, and NRTIs

Drug Interactions Requiring Dose Modifications or Cautious Use			
Drugs Affected	**Nelfinavir (NFV)**	**Amprenavir (APV)**	**Lopinavir(LPV)**
ANTIFUNGALS			
Ketoconazole	No dose adjustment necessary.	Levels: APV ↑ 31% Keto ↑ 44%. Dose: Standard	Levels: LPV AUC ↓ 13%. Keto ↑ 3-fold. Dose: Use with caution; do not exceed 200 mg ketoconazole daily
Voriconazole	No data, but potential for bi-directional inhibition between voriconazole and PIs, monitor for toxicities	No data, but potential for bi-directional inhibition between voriconazole and PIs, monitor for toxicities	No data, but potential for bi-directional inhibition between voriconazole and PIs, monitor for toxicities
ANTI-MYCOBACTERIALS			
Rifampin[Σ]	Levels: NFV ↓ 82%. Should not be coadministered.	Levels: APV AUC ↓ 82% No change in rifampin AUC. Should not be coadministered.	Levels: LPV AUC ↓ 75%. Dose[Σ]: May consider adding 300 mg RTV bid to regimen or ↑ LPV/r to 800/200 mg bid; Rifampin dose standard Increased liver toxicity possible
Rifabutin	Levels: NFV ↓32%. Rifabutin ↑ 2X. Dose: ↓ rifabutin to 150 mg qd or 300 mg 3x/week. ↑ NFV dose to 1000 mg tid.	Levels: APV AUC ↓ 15%. Rifabutin ↑ 193%. Dose: No change in APV dose; Decrease rifabutin to 150 mg qd or 300 mg 3x/week.	Levels: Rifabutin AUC ↑ 3-fold. 25-O-desacetyl metabolite ↑ 47.5-fold. Dose: Decrease rifabutin dose to 150 mg qod; LPV/r: Standard.
Clarithromycin	No data.	Levels: APV AUC ↑ 18%. No change in clarithromycin AUC. No dose adjustment.	Levels: ↑ Clarithromycin AUC 77%. Dose: Adjust for moderate and severe renal impairment.
ORAL CONTRACEPTIVES	Levels: Norethindrone ↓ 18%. Ethinyl estradiol ↓ 47%. Use alternative or additional method.	Levels: Potential for metabolic interactions; use alternative or additional method.	Levels: ethinyl estradiol ↓ 42%. Use alternative or additional method.
LIPID–LOWERING AGENTS			
Simvastatin **Lovastatin**	Avoid concomitant use. Simvistatin AUC ↑ 505%—not recommended. Potential for large increase in Lovastatin AUC—not recommended.	Levels: Potential for large increase in statin levels. Avoid concomitant use.	Levels: Potential for large increase in statin levels. Avoid concomitant use.
Atorvastatin	Atorvastatin AUC ↑ 74%–use with caution and monitor.	Atorvastatin levels have potential for large increase. Use with caution and monitor.	Atorvastatin AUC ↑ 5.88-fold. Use with caution and monitoring.
Pravastatin	No data.	No data.	Pravastatin AUC ↑ 33%; no dosage adjustment necessary
ANTICONVULSANTS			
Carbamazepine **Phenobarbitol** **Phenytoin**	Unknown, but may decrease NFV levels substantially. Monitor anticonvulsant levels.	Unknown, but may decrease APV levels substantially. Monitor anticonvulsant levels.	Many possible interactions: carbamazepine: ↑ levels when co-administered with RTV. Use with caution. Monitor anticonvulsant levels. Phenytoin: ↓ levels of LPV, RTV, and ↓ levels of phenytoin when administered together. Avoid concomitant use.
METHADONE	NFV may decrease methadone levels, but minimal effect on maintenance dose. Monitor and titrate dose if needed. May require ↑ methadone dose.	No data.	Methadone AUC ↓ 53%. Monitor and titrate dose if needed. May require ↑ methadone dose.
SILDENAFIL	Sildenafil AUC ↑ 2-11 fold. Use cautiously. Start with reduced dose of 25 mg every 48 hours and monitor for adverse effects.	Sildenafil AUC ↑ 2-11 fold. Use cautiously. Start with reduced dose of 25 mg every 48 hours and monitor for adverse effects.	Sildenafil AUC ↑ 11-fold in combination with RTV. Use cautiously. Start with reduced dose of 25 mg every 48 hours and monitor for adverse effects.

[Σ] There are limited data on RTV-SQV and RTV-LPV demonstrating that RTV compensates for rifampin induction. In one small study, higher boosting doses or ritonavir (up to 400 mg per dose) were needed to fully offset rifampin-inducing activity of LPV. Whether RTV can be used to offset rifampin induction of all other protease inhibitors, or whether this therapeutic maneuver is more broadly applicable, requires further study.

Table 20: Four Pages

Table 20. Drug Interactions Between Antiretrovirals and Other Drugs: PIs, NNRTIs, and NRTIs

Drug Interactions Requiring Dose Modifications or Cautious Use			
Drugs Affected	**Nevirapine (NVP)**	**Delavirdine (DLV)**	**Efavirenz (EFV)**
ANTIFUNGALS			
Ketoconazole	Levels: Keto. ↓ 63%. NVP ↑ 15-30%. Dose: Not recommended.	No data.	No data.
Voriconazole	No data.	No data.	No data.
ANTI-MYCOBACTERIALS			
Rifampin	Levels: NVP ↓ 37%. Not recommended.	Levels: DLV ↓ 96%. Contraindicated.	Levels: EFV ↓ 25%. Dose: Consider ↑ EFV to 800 mg qd.
Rifabutin	Levels: NVP ↓ 16%. No dose adjustment.*	Levels: DLV ↓ 80%. Rifabutin ↑ 100%. Not recommended.	Levels: EFV unchanged; Rifabutin ↓ 35% Dose: ↑ rifabutin dose to 450-600 mg qd or 600 mg 3x/week.* EFV: Standard
Clarithromycin	Levels: NVP ↑26%. Clarithromycin ↓ 30%. Monitor for efficacy or use alternative agent.	Levels: Clarithromycin ↑100%, DLV ↑ 44%. Dose adjust for renal failure.	Levels: Clarithromycin ↓ 39%. Monitor for efficacy or use alternative agent.
ORAL CONTRACEPTIVES	Levels: ethinyl estradiol ↓ approx 20%. Use alternative or additional methods.	No data.	Levels: Ethinyl estradiol ↑ 37%. No data on other component. Use alternative or additional methods.
LIPID–LOWERING AGENTS			
Simvastatin Lovastatin	No data.	Levels: Potential for large increase in statin levels. Avoid concomitant use.	No data.
Pravastatin	No data.	No data.	No data.
ANTICONVULSANTS			
Carbamazepine Phenobarbitol Phenytoin	Unknown. Use with caution. Monitor anticonvulsant levels.	Unknown, but may decrease DLV levels substantially. Monitor anticonvulsant levels.	Use with caution. Monitor anticonvulsant levels.
METHADONE	Levels: NVP unchanged. Methadone ↓ significantly. Titrate methadone dose to effect.	No data.	Levels: methadone ↓ significantly. Titrate methadone dose to effect.
MISCELLANEOUS	No data.	May increase levels of dapsone, warfarin, and quinidine. Sildenafil: potential for increased concentrations and adverse effects. Use cautiously. Start with reduced dose of 25 mg every 48 hours and monitor for adverse effects.	Monitor warfarin when used concomitantly.

* These recommendations apply to regimens that do not include PIs, which can substantially increase rifabutin levels.

Table 20: Four Pages

Table 20. Drug Interactions Between Antiretrovirals and Other Drugs: PIs, NNRTIs, and NRTIs

Drug Interactions Requiring Dose Modifications or Cautious Use				
Drugs Affected	**Zidovudine (ZDV)**	**Stavudine (d4T)**	**Didanosine (ddI)**	**Tenofovir**
METHADONE	No data.	Levels: d4T ↓ 27%, methadone unchanged. No dose adjustment.	Levels: ddI ↓ 41%, methadone unchanged. Consider ddI dose increase.	No data.
MISCELLANEOUS				
Ribavirin	Ribavirin inhibits phosphorylation of ZDV; this combination should be avoided if possible.	No data.	No data.	No data.
Didanosine buffered tablets	No data.	Peripheral neuropathy, lactic acidosis, and pancreatitis seen with this combination; use with caution and only if potential benefit outweighs potential risks.	No data.	• Levels: ddI AUC ↑ by 44%, Cmax ↑by 28% • Monitor for ddI-associated toxicities • Consider ddI dose reduction.
Cidofovir, Ganciclovir, Valganciclovir	No data.	No data.	No data.	• Possibly competes for active tubular secretion with tenofovir, may increase serum concentration of these drugs and/or tenofovir. • Monitor for dose-related toxicities.